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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/661,358	09/11/2003	Michael Croft	051501-0305443	6765

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Pillsbury Winthrop LLP
Intellectual Property Group
Suite 200
11682 El Camino Real
San Diego, CA 92130-2092

EXAMINER	
OUSPENSKI, ILIA I	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/661,358	CROFT ET AL.	
	Examiner	Art Unit	
	ILIA OUSPENSKI	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 – 4, 6 – 7, 10 – 18, 21 – 31, and 33 – 76* is/are pending in the application.

4a) Of the above claim(s) *10, 12 – 14, 21 – 22, and 40 – 68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 – 4, 6 – 7, 11, 15 – 18, 23 – 31, 33 – 39, and 69 – 76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed on 10/24/2006 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/24/2006 has been entered.

2. Applicant's amendment/remarks, filed on 10/24/2006, are acknowledged.

Claims 5, 8 – 9, 19 – 20, and 32 have been cancelled.

Claims 1 – 4, 6 – 7, 10 – 18, 21 – 31, and 33 – 76 are pending.

Claims 10, 12 – 14, 21 – 22, and 40 – 68 stand withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim.

Claims 1 – 4, 6 – 7, 11, 15 – 18, 23 – 31, 33 – 39, and 69 – 76 are under consideration in the instant application.

3. This Office Action will be in response to applicant's amendment and arguments, filed on 10/24/2006.

The rejections of record can be found in the previous Office Action, mailed on 05/26/2006.

The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

It is noted that New Grounds of Rejection are set forth herein.

4. The objection of record to the oath/declaration has been withdrawn.

5. The following is a quotation of the **first paragraph of 35 U.S.C. 112**:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 74 and 76 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not provide a sufficient enabling description of the claimed methods, wherein the inflammation is "prevented or eliminated."

It is noted that the present rejection is essentially a reiteration of the rejection of record, set forth in the Office Action mailed on 09/26/2005, against claims 71 and 72, which included a recitation of "preventing" language.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification discloses that in a mouse model of asthma, administering a blocking anti-OX40L antibody reduces immune response and inflammation and reduces symptoms of asthma (e.g. Examples 3 – 6 and 9). The instant claims are directed to "preventing or eliminating" inflammation, i.e. completely averting or precluding the development of any aspect of an inflammatory immune response.

Animal model studies have not correlated well with clinical results in patients. Since the therapeutic indices of immunosuppressive biopharmaceuticals, such as costimulation-directed antibodies can be species- and model-dependent, it is not clear that reliance on the disclosed experimental observations provides the basis for predicting the effectiveness of anti-OX40L antibodies in "preventing or eliminating" an inflammatory immune response associated with asthma.

Pharmaceutical therapies in the absence of clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

Further, the burden of enabling the prevention of a manifestation of a disease would be greater than that of enabling a treatment due to the need to screen those humans susceptible to such diseases in the absence of any clinical manifestations, and the difficulty of proof that the administration of the drug was the agent that acted to prevent the condition. Further, the specification does not provide guidance as to how one skilled in the art would go about screening those patients susceptible to asthma within the scope of the presently claimed invention. Nor is guidance provided as to a specific protocol to be utilized in order to prove the efficacy of the presently claimed methods in preventing these disease states. For example, in Basic Facts about Asthma (2003, Centers for Disease Control and Prevention (CDC) Web site; see entire document), CDC states that "in most cases we don't know what causes asthma to develop, and we don't know how to cure asthma" (second paragraph). Further, Mellis (Med. J. Aust., 2002, 177: S78 – S80; see entire document), under the heading "What we need to know," summarizes the knowledge in the art regarding asthma prevention as follows: "Will effective primary prevention require multiple intervention strategies? If so, how feasible are these public health interventions?" Accordingly, undue experimentation is necessary to determine screening and testing protocols to enable the skilled artisan to practice the instantly claimed methods.

7. The Declaration under 37 CFR 1.132 by Dr. Linda Bradley, filed on 10/24/2006, is acknowledged, and has been entered.

8. Regarding Affidavit or Declaration under 37 CFR 1.131 by Drs. Michael Croft and Shaharam Salek-Ardakani, filed on 03/27/2006, the following is noted.

Upon further consideration, the Declaration filed on 03/27/2006 under 37 CFR 1.131 is deemed to be deficient, for the following reasons:

A. The evidence submitted is insufficient to establish applicant's alleged actual reduction to practice of the invention in this country or a NAFTA or WTO member country after the effective date of the cited reference. The declaration does not disclose where the alleged conception or reduction to practice took place.

B. The evidence submitted is insufficient to establish diligence from a date prior to the date of reduction to practice of the cited reference to either a constructive reduction to practice or an actual reduction to practice.

Where conception occurs prior to the date of the reference, but reduction to practice is afterward, it is not enough merely to allege that applicant or patent owner had been diligent. Ex parte Hunter, 1889 C.D. 218, 49 O.G. 733 (Comm'r Pat. 1889). Rather, applicant must show evidence of facts establishing diligence. See MPEP 715.07(a).

9. Claim 1 – 4, 6 – 7, 15 – 18, 23 – 31, 33 – 39, and 69 – 76 stand rejected under **35 U.S.C. 102(e)** as being anticipated by Arndt et al. (US Pat. Pub. No. 2004/0009174; of record; see entire document).

The Declaration by Drs. Michael Croft and Shahram Salek-Ardakani, filed on 03/27/2006 under 37 CFR 1.131, and the Declaration under 37 CFR 1.132 by Dr. Linda Bradley, filed on 10/24/2006, have been considered, but are ineffective to overcome the reference of Arndt et al., for the following reasons:

A. The Declaration by Drs. Michael Croft and Shahram Salek-Ardakani under 37 CFR 1.131 has been found deficient, for the reasons set forth in section 8 supra.

B. The Declaration by Drs. Michael Croft and Shahram Salek-Ardakani under 37 CFR 1.131, when considered together with the Declaration under 37 CFR 1.132 by Dr. Linda Bradley, is not sufficient in scope of disclosure, relative to the scope of the instant claims and the scope of teachings in the prior art.

It is acknowledged that Applicant's amendment has changed the scope of the recited agent from "an agent that reduces or inhibits OX40 or OX40L signaling, expression, or activity" to "an antibody that specifically binds to OX40L," and as such, has obviated the grounds of the rejection of record as they relate to the scope of the agent employed in the claimed methods.

However, scope of the claims as they relate to the condition being treated by the claimed methods is not commensurate with the scope of disclosure provided by the Declarations, when viewed over the prior art of Arndt et al.

The instant claims are directed to a generically recited method of reducing or inhibiting a recall immune response in a mammalian subject, including asthma, by administering an anti-OX40L antibody.

The reference of Arndt et al. broadly teaches methods of reducing inflammation in smooth muscle tissue in a subject (i.e. an immune response), including asthma, by administering the same agent.

The '131 declaration alleges conception of the invention by reference to experiments in a mouse model of asthma. While this disclosure may be sufficient to antedate the teachings of the prior art relative to claims directed to methods of reducing or inhibiting a recall immune response in asthma, it is not sufficient relative to the generic claims of the instant application.

The '132 declaration argues that the studies described in the '131 declaration are representative of recall immune response in general, and inflammation caused by a recall immune response in general.

While not addressing the merits of this assertion, it is noted that possession of one experimental model, even if it were an accepted experimental model for a recall immune response, does not place Applicant in possession of the generically claimed methods, over the broad teachings of the prior art.

Therefore, the rejection of record is maintained for the reasons of record, as it applies to the amended claims. The rejection or record is incorporated by reference herein, as if reiterated in full.

10. Claims 1 and 11 stand rejected under **35 U.S.C. 103(a)** as being unpatentable over Arndt et al. (US Pat. Pub. No. 2004/0009174; see entire document) in view of Owens et al. (Journal of Immunological Methods, 1994, 168: 149 - 165; see entire document).

Applicant relies on the Declarations under 37 CFR 1.131 and 1.132 to argue that the reference of Arndt et al. is not available as prior art against the instant claims.

Applicant's arguments have been addressed in section 9, supra, and have not been found sufficiently persuasive. Therefore, the rejection of record is maintained for the reasons of record, as it applies to the amended claims. The rejection or record is incorporated by reference herein, as if reiterated in full.

11. Conclusion: no claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is 571-272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ILIA OUSPENSKI, Ph.D.
Patent Examiner
Art Unit 1644

PHILLIP CAMPBELL, PH.D
PRIMARY EXAMINER
TC 1600

December 28, 2006